Clinical trial results:
Safety, efficacy and exposure of subcutaneously administered NNC0365-3769 (Mim8) prophylaxis in children with haemophilia A with or without FVIII inhibitors

Summary

EudraCT number	2020-003467-26
Trial protocol	NL PL IT ES PT LT
Global end of trial date	13 November 2024

Results information

Result version number	v1 (current)
This version publication date	28 May 2025
First version publication date	28 May 2025

Trial information

Trial identification

Sponsor protocol code	NN7769-4516

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05306418
WHO universal trial number (UTN)	U1111-1255-1540
Other trial identifiers	Japanese trial registration number: jRCT2031220670

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002762-PIP02-02
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 January 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 November 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the safety of Mim8 prophylaxis in children with haemophilia A with or without coagulation factor VIII (FVIII) inhibitors.

Protection of trial subjects:

This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki, applicable International Council for Harmonization (ICH) Good Clinical Practice guidelines, and other applicable laws and regulations.

Background therapy:

The products/treatment used for bleeds and surgery and prophylactic treatment during run-in period, treatment period and the follow-up period were regarded as non-investigational medicinal products (non-IMPs) in this trial. Prophylactic use of standard and extended FVIII products could continue for 1 week after Mim8 loading dose.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	04 April 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	China: 10
Country: Number of subjects enrolled	India: 9
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Japan: 1
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	South Africa: 7
Country: Number of subjects enrolled	Korea, Republic of: 9
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 6

Worldwide total number of subjects	71
EEA total number of subjects	18

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	10
Children (2-11 years)	61
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 29 sites that recruited subjects in Canada, China, India, Israel, Italy, Japan, Netherlands, Poland, Portugal, South Africa, South Korea, Spain, Switzerland, Taiwan, United Kingdom and United States.

Pre-assignment

Screening details:

Study included run-in period of at least 26 weeks for children previously treated on prophylaxis (PPX) which was followed by 52-week treatment period with part 1 + part 2, where all subjects received Mim8 and 21-week follow-up period unless the subject or parent(s)/caregiver(s) wanted to transfer to open-label extension study NN7769-4532.

Period 1

Period 1 title	Treatment Period - Part 1
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Mim8 Once Weekly - Subjects 1-5 years

Arm description:

Subjects aged 1-5 years subcutaneously received Mim8 once weekly based on their weight band until week-26 in part 1.

Arm type	Experimental
Investigational medicinal product name	Mim8
Investigational medicinal product code	NNC0365 -3769 B
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose was administered once followed by once weekly maintenance doses in part 1. Loading doses were administered by 1 or 2 injections, using 1 or 2 cartridges of study intervention. Maintenance doses were administered by 1 injection using 1 cartridge of study intervention. 0.8 milliliter (mL) of study intervention was administered per injection. Dose amount was based on weight band of subject, whether it was a loading or maintenance dose, and the frequency of dosing: total loading dose (9.0 milligrams [mg] for less than 15 kilograms (kg), 24.0 mg for equals 15 kg - less than 45 kg and 55.0 mg for greater than equals 45 kg); total maintenance dose (1.6 mg for less than 15 kg, 4.0 mg for equals 15 kg - less than 45 kg and 9.0 mg greater than equals 45 kg).

Arm title	Part 1: Mim8 Once Weekly - Subjects 6-11 years

Arm description:

Subjects aged 6-11 years subcutaneously received Mim8 once weekly subcutaneously based on their weight band until week-26 in part 1.

Arm type	Experimental
Investigational medicinal product name	Mim8
Investigational medicinal product code	NNC0365 -3769 B
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose was administered once followed by once weekly maintenance doses in part 1. Loading doses were administered by 1 or 2 injections, using 1 or 2 cartridges of study intervention. Maintenance doses were administered by 1 injection using 1 cartridge of study intervention. 0.8 milliliter (mL) of

study intervention was administered per injection. Dose amount was based on weight band of subject, whether it was a loading or maintenance dose, and the frequency of dosing: total loading dose (9.0 milligrams [mg] for less than 15 kilograms (kg), 24.0 mg for equals 15 kg - less than 45 kg and 55.0 mg for greater than equals 45 kg); total maintenance dose (1.6 mg for less than 15 kg, 4.0 mg for equals 15 kg - less than 45 kg and 9.0 mg greater than equals 45 kg).

Number of subjects in period 1[1]	Part 1: Mim8 Once Weekly - Subjects 1-5 years	Part 1: Mim8 Once Weekly - Subjects 6-11 years
Started	36	34
Completed	36	34

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The total of 71 subjects enrolled in the study. Out of 71 subjects, 1 subject withdrew during run-in period. Hence, data are reported for 70 participants.

Period 2

Period 2 title	Treatment Period - Part 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 2: Mim8 Once Weekly - Subjects 1-5 years

Arm description:

Subjects aged 1-5 years from part 1, decided at week-26 to continue on subcutaneously Mim8 once weekly (dose amount based on their weight band) until week-52 in part 2. The part 2 treatment period was followed by a 21-week follow-up period for all subjects unless the subjects or the parent(s)/caregiver(s) wanted to transfer to the open-label extension study NN7769-4532.

Arm type	Experimental
Investigational medicinal product name	Mim8
Investigational medicinal product code	NNC0365 -3769 B
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Doses were administered once weekly in part 2. Doses were administered by 1 injection using 1 cartridge of study intervention. 0.8 mL of study intervention was administered per injection. Dose amount was based on weight band of subject, total dose (1.6 mg for less than 15 kg, 4.0 mg for equals 15 kg - less than 45 kg and 9.0 mg greater than equals 45 kg).

Arm title	Part 2: Mim8 Once Weekly - Subjects 6-11 years

Arm description:

Subjects aged 6-11 years from part 1, decided at week-26 to continue on subcutaneously Mim8 once weekly (dose amount based on their weight band) until week-52 in part 2. The part 2 treatment period was followed by a 21-week follow-up period for all subjects unless the subjects or the parent(s)/caregiver(s) wanted to transfer to the open-label extension study NN7769-4532.

Arm type	Experimental

Investigational medicinal product name	Mim8
Investigational medicinal product code	NNC0365 -3769 B
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Doses were administered once weekly in part 2. Doses were administered by 1 injection using 1 cartridge of study intervention. 0.8 mL of study intervention was administered per injection. Dose amount was based on weight band of subject, total dose (1.6 mg for less than 15 kg, 4.0 mg for equals 15 kg - less than 45 kg and 9.0 mg greater than equals 45 kg).

Arm title	Part 2: Mim8 Once Monthly - Subjects 1-5 years

Arm description:

Subjects aged 1-5 years from part 1, decided at week-26 to switch to subcutaneously Mim8 once monthly (dose amount based on their weight band) until week-52 in part 2. The part 2 treatment period was followed by a 21-week follow-up period for all subjects unless the subjects or the parent(s)/caregiver(s) wanted to transfer to the open-label extension study NN7769-4532.

Arm type	Experimental
Investigational medicinal product name	Mim8
Investigational medicinal product code	NNC0365 -3769 B
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Doses were administered once monthly in part 2. Doses were administered by 1 injection using 1 cartridge of study intervention. 0.8 mL of study intervention was administered per injection. Dose amount was based on weight band of subject, total dose (9.0 mg for less than 15 kg, 20.0 mg for equals 15 kg - less than 45 kg and 46.0 mg greater than equals 45 kg).

Arm title	Part 2: Mim8 Once Monthly - Subjects 6-11 years

Arm description:

Subjects aged 6-11 years from part 1, decided at week-26 to switch to subcutaneously Mim8 once monthly (dose amount based on their weight band) until week-52 in part 2. The part 2 treatment period was followed by a 21-week follow-up period for all subjects unless the subjects or the parent(s)/caregiver(s) wanted to transfer to the open-label extension study NN7769-4532.

Arm type	Experimental
Investigational medicinal product name	Mim8
Investigational medicinal product code	NNC0365 -3769 B
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Doses were administered once monthly in part 2. Doses were administered by 1 injection using 1 cartridge of study intervention. 0.8 mL of study intervention was administered per injection. Dose amount was based on weight band of subject, total dose (9.0 mg for less than 15 kg, 20.0 mg for equals 15 kg - less than 45 kg and 46.0 mg greater than equals 45 kg).

Number of subjects in period 2	Part 2: Mim8 Once Weekly - Subjects 1-5 years	Part 2: Mim8 Once Weekly - Subjects 6-11 years	Part 2: Mim8 Once Monthly - Subjects 1-5 years
Started	19	19	17
Completed	19	19	17

Number of subjects in period 2	Part 2: Mim8 Once Monthly - Subjects 6-11 years
Started	15
Completed	15

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: Mim8 Once Weekly - Subjects 1-5 years
Reporting group description:	
Subjects aged 1-5 years subcutaneously received Mim8 once weekly based on their weight band until week-26 in part 1.	
Reporting group title	Part 1: Mim8 Once Weekly - Subjects 6-11 years
Reporting group description:	
Subjects aged 6-11 years subcutaneously received Mim8 once weekly subcutaneously based on their weight band until week-26 in part 1.	

Reporting group values	Part 1: Mim8 Once Weekly - Subjects 1-5 years	Part 1: Mim8 Once Weekly - Subjects 6-11 years	Total
Number of subjects	36	34	70
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	2.9	8.4	
standard deviation	± 1.4	± 1.9	-
Gender Categorical Units: subjects			
Male	36	34	70

End points

End points reporting groups

Reporting group title	Part 1: Mim8 Once Weekly - Subjects 1-5 years

Reporting group description:

Subjects aged 1-5 years subcutaneously received Mim8 once weekly based on their weight band until week-26 in part 1.

Reporting group title	Part 1: Mim8 Once Weekly - Subjects 6-11 years

Reporting group description:

Subjects aged 6-11 years subcutaneously received Mim8 once weekly subcutaneously based on their weight band until week-26 in part 1.

Reporting group title	Part 2: Mim8 Once Weekly - Subjects 1-5 years

Reporting group description:

Subjects aged 1-5 years from part 1, decided at week-26 to continue on subcutaneously Mim8 once weekly (dose amount based on their weight band) until week-52 in part 2. The part 2 treatment period was followed by a 21-week follow-up period for all subjects unless the subjects or the parent(s)/caregiver(s) wanted to transfer to the open-label extension study NN7769-4532.

Reporting group title	Part 2: Mim8 Once Weekly - Subjects 6-11 years

Reporting group description:

Subjects aged 6-11 years from part 1, decided at week-26 to continue on subcutaneously Mim8 once weekly (dose amount based on their weight band) until week-52 in part 2. The part 2 treatment period was followed by a 21-week follow-up period for all subjects unless the subjects or the parent(s)/caregiver(s) wanted to transfer to the open-label extension study NN7769-4532.

Reporting group title	Part 2: Mim8 Once Monthly - Subjects 1-5 years

Reporting group description:

Subjects aged 1-5 years from part 1, decided at week-26 to switch to subcutaneously Mim8 once monthly (dose amount based on their weight band) until week-52 in part 2. The part 2 treatment period was followed by a 21-week follow-up period for all subjects unless the subjects or the parent(s)/caregiver(s) wanted to transfer to the open-label extension study NN7769-4532.

Reporting group title	Part 2: Mim8 Once Monthly - Subjects 6-11 years

Reporting group description:

Subjects aged 6-11 years from part 1, decided at week-26 to switch to subcutaneously Mim8 once monthly (dose amount based on their weight band) until week-52 in part 2. The part 2 treatment period was followed by a 21-week follow-up period for all subjects unless the subjects or the parent(s)/caregiver(s) wanted to transfer to the open-label extension study NN7769-4532.

Subject analysis set title	Part 1+2: Mim8 Once Weekly - Subjects 1-5 years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects aged 1-5 years subcutaneously received Mim8 once weekly until week-26 in part 1. For the part 2, a subgroup of patients decided at week-26 to continue on Mim8 once weekly until week-52 in part 2. The part 2 treatment period was followed by a 21-week follow-up period for all subjects unless the subjects or the parent(s)/caregiver(s) wanted to transfer to the open-label extension study NN7769-4532.

Subject analysis set title	Part 1+2: Mim8 Once Weekly - Subjects 6-11 years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects aged 6-11 years subcutaneously received Mim8 once weekly until week-26 in part 1. For the part 2, a subgroup of patients decided at week-26 to continue on Mim8 once weekly until week-52 in part 2. The part 2 treatment period was followed by a 21-week follow-up period for all subjects unless the subjects or the parent(s)/caregiver(s) wanted to transfer to the open-label extension study NN7769-4532.

Subject analysis set title	Run-in: Previous PPX + Previous On Demand Subjects 1-5 years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects aged 1-5 years previously treated on prophylaxis (standard/extended half-life FVIII or bypassing agent) or on demand participated in run-in period.

Subject analysis set title	Run-in: Previous PPX + Previous On Demand Subjects 6-11 years
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects aged 6-11 years previously treated on prophylaxis (standard/extended half-life FVIII or bypassing agent) or on demand participated in run-in period.

Primary: Number of treatment emergent adverse events (TEAEs)

End point title	Number of treatment emergent adverse events (TEAEs)[1]

End point description:

AE is any untoward medical occurrence in a subject that is temporally associated with the use of an IMP, whether or not considered related to IMP. Number of TEAEs is presented. AEs were evaluated based on data from on-treatment period which is given as time period in which subject was exposed to trial product and started at the date of first dose of product and ended at the first date of any of the following: end of treatment visit if they enrolled in the study NN7769-4532 or follow-up visit and last date on trial product +21 weeks. Safety analysis set (SAS) included all subjects exposed to at least 1 dose of trial product and were analysed according to treatment they actually received. As defined in protocol section 9, analysis was planned to be performed for once weekly and once monthly treatment regimens. Hence, all of subjects during part 1 as well as that decided to continue on Mim8 once weekly in part 2 are combined and represented in part 1+2 once weekly reporting group.

End point type	Primary

End point timeframe:

From treatment initiation to follow up visit (week 0 to week 72)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary endpoint investigated safety and was analysed using descriptive statistics, and thus no statistical analysis was performed.

End point values	Part 2: Mim8 Once Monthly - Subjects 1-5 years	Part 2: Mim8 Once Monthly - Subjects 6-11 years	Part 1+2: Mim8 Once Weekly - Subjects 1-5 years	Part 1+2: Mim8 Once Weekly - Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	15	36	34
Units: events	20	27	99	85

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treated bleeds

End point title	Number of treated bleeds

End point description:

A bleed is considered treated if a coagulation factor product is administered to stop the bleed. Number of treated bleeds are presented. The endpoint was evaluated based on in-study period. The in-study period started at the first dose of Mim8 or screening (for run-in) and ended at the end of treatment period or discontinuation of Mim8. Analysis population (full analysis set [FAS]) included all subjects exposed to at least 1 dose of trial product. Subjects were analysed according to the treatment they actually received. As defined in protocol section 9, analysis was planned to be performed for once weekly and once monthly treatment regimens. Hence, all of subjects during part 1 as well as that decided to continue on Mim8 once weekly in part 2 are combined and represented in part 1+2 once weekly reporting group.

End point type	Secondary

End point timeframe:

From treatment initiation to end of treatment (week 0 to week 52)

End point values	Part 2: Mim8 Once Monthly - Subjects 1-5 years	Part 2: Mim8 Once Monthly - Subjects 6-11 years	Part 1+2: Mim8 Once Weekly - Subjects 1-5 years	Part 1+2: Mim8 Once Weekly - Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	15	36	34
Units: bleeds	2	2	15	20

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treated spontaneous bleeds

End point title	Number of treated spontaneous bleeds

End point description:

A bleed is considered treated if a coagulation factor product is administered to stop the bleed. A spontaneous bleed refers bleeding instance that occur without a clear cause or not linked to a specific, known event or activity. Number of treated spontaneous bleeds are presented. The endpoint was evaluated based on in-study period. The in-study period started at the first dose of Mim8 or screening (for run-in) and ended at the end of treatment period or discontinuation of Mim8. FAS included all subjects exposed to at least 1 dose of trial product. Subjects were analysed according to the treatment they actually received. As defined in protocol section 9, analysis was planned to be performed for once weekly and once monthly treatment regimens. Hence, all of subjects during part 1 as well as that decided to continue on Mim8 once weekly in part 2 are combined and represented in part 1+2 once weekly reporting group.

End point type	Secondary

End point timeframe:

From treatment initiation to end of treatment (week 0 to week 52)

End point values	Part 2: Mim8 Once Monthly - Subjects 1-5 years	Part 2: Mim8 Once Monthly - Subjects 6-11 years	Part 1+2: Mim8 Once Weekly - Subjects 1-5 years	Part 1+2: Mim8 Once Weekly - Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	15	36	34
Units: bleeds	0	1	2	3

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treated joint bleeds

End point title	Number of treated joint bleeds

End point description:

A bleed is considered treated if a coagulation factor product is administered to stop the bleed. A joint bleed refers bleeding instance that is caused in joints. Number of treated joints bleeds are presented. The endpoint was evaluated based on in-study period. The in-study period started at the first dose of Mim8 or screening (for run-in) and ended at the end of treatment period or discontinuation of Mim8. FAS included all subjects exposed to at least 1 dose of trial product. Subjects were analysed according to the treatment they actually received. As defined in protocol section 9, analysis was planned to be performed for once weekly and once monthly treatment regimens. Hence, all of subjects during part 1 as well as that decided to continue on Mim8 once weekly in part 2 are combined and represented in part 1+2 once weekly reporting group.

End point type	Secondary

End point timeframe:

From treatment initiation to end of treatment (week 0 to week 52)

End point values	Part 2: Mim8 Once Monthly - Subjects 1-5 years	Part 2: Mim8 Once Monthly - Subjects 6-11 years	Part 1+2: Mim8 Once Weekly - Subjects 1-5 years	Part 1+2: Mim8 Once Weekly - Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	15	36	34
Units: bleeds	0	2	3	12

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treated traumatic bleeds

End point title	Number of treated traumatic bleeds

End point description:

A bleed is considered treated if a coagulation factor product is administered to stop the bleed. A traumatic bleed refers bleeding instance that is caused by a specific, known event or activity (e.g. injury or exercise). Number of treated traumatic bleeds are presented. The endpoint was evaluated based on in-study period. The in-study period started at the first dose of Mim8 or screening (for run-in) and ended at the end of treatment period or discontinuation of Mim8. FAS included all subjects exposed to at least 1 dose of trial product. Subjects were analysed according to the treatment they actually received. As defined in protocol section 9, analysis was planned to be performed for once weekly and once monthly treatment regimens. Hence, all of subjects during part 1 as well as that decided to continue on Mim8 once weekly in part 2 are combined and represented in part 1+2 once weekly reporting group.

End point type	Secondary

End point timeframe:

From treatment initiation to end of treatment (week 0 to week 52)

End point values	Part 2: Mim8 Once Monthly - Subjects 1-5 years	Part 2: Mim8 Once Monthly - Subjects 6-11 years	Part 1+2: Mim8 Once Weekly - Subjects 1-5 years	Part 1+2: Mim8 Once Weekly - Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	15	36	34
Units: bleeds	2	1	12	16

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treated target joint bleeds

End point title	Number of treated target joint bleeds

End point description:

A bleed is considered treated if a coagulation factor product is administered to stop the bleed. A target joint is defined as a joint in which 3 or more spontaneous bleeding episodes have occurred within 6 months before the date of the assessment. Number of treated target joints bleeds are presented. The endpoint was evaluated based on in-study period. The in-study period started at the first dose of Mim8 or screening (for run-in) and ended at the end of treatment period or discontinuation of Mim8. FAS included all subjects exposed to at least 1 dose of trial product. Subjects were analysed according to the treatment they actually received. As defined in protocol section 9, analysis was planned to be performed for once weekly and once monthly treatment regimens. Hence, all of subjects during part 1 as well as that decided to continue on Mim8 once weekly in part 2 are combined and represented in part 1+2 once weekly reporting group.

End point type	Secondary

End point timeframe:

From treatment initiation to end of treatment (week 0 to week 52)

End point values	Part 2: Mim8 Once Monthly - Subjects 1-5 years	Part 2: Mim8 Once Monthly - Subjects 6-11 years	Part 1+2: Mim8 Once Weekly - Subjects 1-5 years	Part 1+2: Mim8 Once Weekly - Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	15	36	34
Units: bleeds	0	0	0	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of injection site reactions

End point title	Number of injection site reactions

End point description:

Injection site reactions were assessed based on subject feedback and visual inspection of injection site. Number of injection site reactions are presented. Endpoint was evaluated based on data from on-treatment period. The on-treatment period represented the time period in which a subject was

considered exposed to trial product and started at the date of first dose of trial product and ended at the first date of any of the following: end of treatment visit if they enrolled in the study NN7769-4532 or the follow-up visit and the last date on trial product + 21 weeks. SAS included all subjects exposed to at least 1 dose of trial product and were analysed according to the treatment they actually received. As defined in protocol section 9, analysis was planned to be performed for once weekly and once monthly treatment regimens. Hence, all of subjects during part 1 as well as that decided to continue on Mim8 once weekly in part 2 are combined and represented in part 1+2 once weekly group.

End point type	Secondary

End point timeframe:

From treatment initiation to end of treatment (week 0 to week 52)

End point values	Part 2: Mim8 Once Monthly - Subjects 1-5 years	Part 2: Mim8 Once Monthly - Subjects 6-11 years	Part 1+2: Mim8 Once Weekly - Subjects 1-5 years	Part 1+2: Mim8 Once Weekly - Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	15	36	34
Units: site reactions	0	5	6	20

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of anti-Mim8 antibodies

End point title	Occurrence of anti-Mim8 antibodies

End point description:

Number of subjects with anti-Mim8 antibodies are presented. The endpoint was evaluated based on data from on-treatment period. The on-treatment period represented the time period in which a subject was considered exposed to trial product and started at the date of first dose of trial product and ended at the first date of any of the following: end of treatment visit if they enrolled in the study NN7769-4532 or the follow-up visit and the last date on trial product + 21 weeks. SAS included all subjects exposed to at least 1 dose of trial product. Subjects were analysed according to the treatment they actually received. As defined in protocol section 9, analysis was planned to be performed for once weekly and once monthly treatment regimens. Hence, all of subjects during part 1 as well as that decided to continue on Mim8 once weekly in part 2 are combined and represented in part 1+2 once weekly reporting group.

End point type	Secondary

End point timeframe:

From treatment initiation to end of treatment (week 0 to week 52)

End point values	Part 2: Mim8 Once Monthly - Subjects 1-5 years	Part 2: Mim8 Once Monthly - Subjects 6-11 years	Part 1+2: Mim8 Once Weekly - Subjects 1-5 years	Part 1+2: Mim8 Once Weekly - Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	15	36	34
Units: subjects	0	0	1	4

Statistical analyses

No statistical analyses for this end point

Secondary: Consumption of factor product per bleed treatment (number of injections per bleed)

End point title	Consumption of factor product per bleed treatment (number of injections per bleed)

End point description:

Consumption of factor product per bleed treatment was calculated as number of injections used in the time period from the start of bleed to the stop of bleed. The mean number of injections required to stop the bleed is presented. The analysis was based on the total number of bleeds. The endpoint was evaluated based on in-study period. The in-study period starts at the first dose of Mim8 or screening (for run-in) and ends at the end of treatment period or discontinuation of Mim8. For subjects with run-in, the in-study period starts at screening and ends at the end of treatment period or discontinuation of Mim8. FAS included all subjects exposed to at least 1 dose of trial product. Subjects were analysed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

From run-in initiation to end of treatment (week -26 to week 52)

End point values	Part 1: Mim8 Once Weekly - Subjects 1-5 years	Part 2: Mim8 Once Weekly - Subjects 1-5 years	Part 1: Mim8 Once Weekly - Subjects 6-11 years	Part 2: Mim8 Once Weekly - Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	19	34	19
Units: injections per bleed				
arithmetic mean (standard deviation)	1.0 (± 0.0)	1.0 (± 0.0)	1.4 (± 0.8)	1.3 (± 0.6)

End point values	Part 2: Mim8 Once Monthly - Subjects 1-5 years	Part 2: Mim8 Once Monthly - Subjects 6-11 years	Run-in: Previous PPX + Previous On Demand Subjects 1-5 years	Run-in: Previous PPX + Previous On Demand Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	17	15	19	19
Units: injections per bleed				
arithmetic mean (standard deviation)	1.0 (± 0.0)	1.5 (± 0.7)	1.1 (± 0.3)	1.3 (± 0.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Mim8 plasma concentration

End point title	Mim8 plasma concentration

End point description:

The endpoint was evaluated based on in-study period. The in-study period started at the first dose of Mim8 or screening (for run-in) and ended at the end of treatment period or discontinuation of Mim8. FAS included all subjects exposed to at least 1 dose of trial product. Subjects were analysed according to the treatment they actually received. Here, "n" represents number of subjects who evaluable at specific time point for respective reporting group and "99999" indicates not applicable data point.

End point type	Secondary

End point timeframe:

From treatment initiation to end of treatment (week 0 to week 52)

End point values	Part 1: Mim8 Once Weekly - Subjects 1-5 years	Part 2: Mim8 Once Weekly - Subjects 1-5 years	Part 1: Mim8 Once Weekly - Subjects 6-11 years	Part 2: Mim8 Once Weekly - Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	19	34	19
Units: microgram per milliliter (µg/mL)				
arithmetic mean (standard deviation)				
Week 0(n=33,34,0,0,0,0)	0.0 (± 0.0)	99999 (± 99999)	0.0 (± 0.0)	99999 (± 99999)
Week 26 (n=35,34,0,0,0,0)	6.81 (± 2.43)	99999 (± 99999)	5.07 (± 1.98)	99999 (± 99999)
Week 36 (n=0,0,19,19,17,15)	99999 (± 99999)	6.77 (± 2.41)	99999 (± 99999)	4.36 (± 1.40)
Week 52 (n=0,0,19,19,16,15)	99999 (± 99999)	6.18 (± 2.02)	99999 (± 99999)	4.13 (± 1.63)

End point values	Part 2: Mim8 Once Monthly - Subjects 1-5 years	Part 2: Mim8 Once Monthly - Subjects 6-11 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	15		
Units: microgram per milliliter (µg/mL)				
arithmetic mean (standard deviation)				
Week 0(n=33,34,0,0,0,0)	99999 (± 99999)	99999 (± 99999)		
Week 26 (n=35,34,0,0,0,0)	99999 (± 99999)	99999 (± 99999)		
Week 36 (n=0,0,19,19,17,15)	6.97 (± 3.02)	5.22 (± 1.62)		
Week 52 (n=0,0,19,19,16,15)	4.01 (± 1.33)	4.03 (± 1.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment preference for Mim8 versus previous treatment using Caregiver Haemophilia Patient Preference Questionnaire (Caregiver H-PPQ)

End point title	Treatment preference for Mim8 versus previous treatment using Caregiver Haemophilia Patient Preference Questionnaire (Caregiver H-PPQ)

End point description:

The questionnaire assesses "Overall which treatment do you prefer?", with the response options "current", "previous" or "no preference", and "How strong is that preference", with the response options "very strong", "fairly strong", and "not very strong". Percentage of subjects with treatment preference for Mim8 versus previous treatment using caregiver H-PPQ is presented. The caregiver H-PPQ is only relevant for previously treated subjects. The endpoint was evaluated based on in-study period. The in-study period started at the first dose of Mim8 or screening (for run-in) and ended at the end of treatment period or discontinuation of Mim8. FAS included all subjects exposed to at least 1 dose of trial product. Subjects were analysed according to the treatment they actually received. Here, "number of subjects analysed" included subjects who had responded the questionnaire within a 1 day interval and applicable for previously treated subjects at week 26.

End point type	Secondary

End point timeframe:

Once during treatment (week 26)

End point values	Part 1: Mim8 Once Weekly - Subjects 1-5 years	Part 1: Mim8 Once Weekly - Subjects 6-11 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	30		
Units: percentage of subjects				
number (not applicable)				
Current treatment: Very strong	76.7	70.0		
Current treatment: Fairly strong	20.0	23.3		
Current treatment: Not very strong	3.3	3.3		
Previous treatment	0	0		
No preference	0	3.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in physical function domain of Paediatric Quality of Life inventory (PEDS-QL) Generic Core Scales

End point title	Change in physical function domain of Paediatric Quality of Life inventory (PEDS-QL) Generic Core Scales

End point description:

PedsQL assesses quality of life, including domains like physical functioning. Higher scores indicate better quality of life and physical functioning with range from 0-100. Positive change indicates improvement and negative change indicates worsening. Questionnaire is for 5 to 11 years. Change in PEDS-QL from week 0 to week 52 is presented. Endpoint based on in-study period which started at first dose of Mim8 or screening (for run-in) and ended at end of treatment or discontinuation of Mim8. FAS included

subjects exposed to at least 1 dose of trial product and analysed based on treatment they actually received. In protocol section 9, analysis was planned to be performed for once weekly and once monthly treatment regimens. Hence, all of subjects during part 1 as well as that decided to continue on Mim8 once weekly in part 2 are combined and represented in part 1+2 once weekly group. Here, "subject analysed" included responders at week 0 and week 52 and "99999" indicates not applicable.

End point type	Secondary

End point timeframe:

From treatment initiation to end of treatment (week 0 to week 52)

End point values	Part 2: Mim8 Once Monthly - Subjects 1-5 years	Part 2: Mim8 Once Monthly - Subjects 6-11 years	Part 1+2: Mim8 Once Weekly - Subjects 1-5 years	Part 1+2: Mim8 Once Weekly - Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	1	12	3	13
Units: score on a scale				
arithmetic mean (standard deviation)	0.0 (± 99999)	7.0 (± 13.1)	-1.0 (± 1.8)	23.8 (± 18.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in subjects' treatment burden using the Haemophilia treatment experience measure (Hemo TEM)

End point title	Change in subjects' treatment burden using the Haemophilia treatment experience measure (Hemo TEM)

End point description:

Child Hemo-TEM (caregiver reported) measures treatment burden. Change in subjects' treatment burden using Hemo TEM from week 0 to week 52 is presented. The score ranges from 0-100 where lower score indicates lower treatment burden. The caregiver H-PPQ is only relevant for previously treated subjects. Endpoint was evaluated based on in-study period. The in-study period started at the first dose of Mim8 or screening (run-in) and ended at the end of treatment period or discontinuation of Mim8. FAS included all subjects exposed to at least 1 dose of trial product. Subjects were analysed according to the treatment they actually received. In protocol section 9, analysis was planned to be performed for once weekly and once monthly treatment regimens. Hence, all of subjects during part 1 as well as that decided to continue on Mim8 once weekly in part 2 are combined and represented in part 1+2 once weekly reporting group. Here, "subject analysed" includes responders at week 0 and week 52.

End point type	Secondary

End point timeframe:

From treatment initiation to end of treatment (week 0 to week 52)

End point values	Part 2: Mim8 Once Monthly - Subjects 1-5 years	Part 2: Mim8 Once Monthly - Subjects 6-11 years	Part 1+2: Mim8 Once Weekly - Subjects 1-5 years	Part 1+2: Mim8 Once Weekly - Subjects 6-11 years
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	10	12	14	13
Units: score on a scale				

arithmetic mean (standard deviation)	-14.6 (± 14.3)	-19.6 (± 15.3)	-13.0 (± 25.0)	-26.9 (± 28.7)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From treatment initiation to follow up visit (week 0 to week 72)

Adverse event reporting additional description:

Based on on-treatment period - period started at the date of first dose and ended at the first date of any of following: end of treatment if they enrolled in NN7769-4532 or follow-up and last date on trial product +21 weeks. SAS included all subjects exposed to at least 1 dose of trial product and based on treatment they actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Part 1+2: Mim8 - Subjects 6-11 years

Reporting group description:

All subjects aged 6-11 years received subcutaneously Mim8 once weekly in part 1 and part 2 or once weekly in part 1 and once monthly in part 2 from week 0 until week 52. The part 2 treatment period was followed by a 21-week follow-up period for all subjects unless the subjects or the parent(s)/caregiver(s) wanted to transfer to the open-label extension study NN7769-4532.

Reporting group title	Part 1+2: Mim8 - Subjects 1-5 years

Reporting group description:

All subjects aged 1-5 years received subcutaneously Mim8 once weekly in part 1 and part 2 or once weekly in part 1 and once monthly in part 2 from week 0 until week 52. The part 2 treatment period was followed by a 21-week follow-up period for all subjects unless the subjects or the parent(s)/caregiver(s) wanted to transfer to the open-label extension study NN7769-4532.

Serious adverse events	Part 1+2: Mim8 - Subjects 6-11 years	Part 1+2: Mim8 - Subjects 1-5 years	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 34 (11.76%)	1 / 36 (2.78%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 34 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Myositis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycoplasma infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	1 / 34 (2.94%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis streptococcal			
subjects affected / exposed	1 / 34 (2.94%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia haemophilus			
subjects affected / exposed	1 / 34 (2.94%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Part 1+2: Mim8 - Subjects 6-11 years	Part 1+2: Mim8 - Subjects 1-5 years	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 34 (67.65%)	30 / 36 (83.33%)	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 34 (5.88%)	0 / 36 (0.00%)	
occurrences (all)	3	0	
Prothrombin fragment 1.2 increased			
subjects affected / exposed	6 / 34 (17.65%)	3 / 36 (8.33%)	
occurrences (all)	7	4	
Fibrin D dimer increased			

subjects affected / exposed	0 / 34 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 34 (5.88%)	2 / 36 (5.56%)	
occurrences (all)	3	2	
Skin laceration			
subjects affected / exposed	2 / 34 (5.88%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
Product communication issue			
subjects affected / exposed	2 / 34 (5.88%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 34 (2.94%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	2 / 34 (5.88%)	5 / 36 (13.89%)	
occurrences (all)	25	6	
Pyrexia			
subjects affected / exposed	5 / 34 (14.71%)	9 / 36 (25.00%)	
occurrences (all)	5	10	
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	0 / 34 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Vomiting			
subjects affected / exposed	2 / 34 (5.88%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 34 (11.76%)	5 / 36 (13.89%)	
occurrences (all)	4	5	
Skin and subcutaneous tissue disorders			

Dermatitis contact			
subjects affected / exposed	0 / 34 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 34 (0.00%)	4 / 36 (11.11%)	
occurrences (all)	0	4	
Upper respiratory tract infection			
subjects affected / exposed	6 / 34 (17.65%)	9 / 36 (25.00%)	
occurrences (all)	6	10	
Influenza			
subjects affected / exposed	1 / 34 (2.94%)	3 / 36 (8.33%)	
occurrences (all)	1	3	
Nasopharyngitis			
subjects affected / exposed	4 / 34 (11.76%)	2 / 36 (5.56%)	
occurrences (all)	5	5	
Respiratory tract infection			
subjects affected / exposed	0 / 34 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 34 (0.00%)	3 / 36 (8.33%)	
occurrences (all)	0	4	
Viral infection			
subjects affected / exposed	2 / 34 (5.88%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
Varicella			
subjects affected / exposed	0 / 34 (0.00%)	3 / 36 (8.33%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 June 2021	Amended to extend the follow-up period from 16 to 21 weeks after last dose; to clarify inclusion criterion 4 - it will be assessed by checking if the subject had a prescription of FVIII concentrate or bypassing agent; correction to align with the study design, as subjects treated on demand have the option to have a run-in period; Correction to specify that the target joints only need be assessed at week 4; to specify that clinical safety data from the phase 1 study will be summarised before this study will be initiated and that the summary will be submitted to regulatory authorities if and as required.
26 August 2021	Amended to add statement to clarify children under which age group are allowed for the first 10 subjects to be dosed in the study; in order to describe the involvement of data monitoring committee (DMC) in decisions regarding study and confirmation of the role of DMC in the study.
22 August 2022	Amended to include the dose for subjects based on the multiple ascending dose (MAD) part of study NN7769-4513 and on study NN7769-4882; exclusion criterion updated regarding requirement of participation in any interventional clinical study prior to this study; exclusion criterion updated regarding exposure to non-factor haemostatic products; to comply with section about concomitant medication; updated sections based on interim CTR from study NN7769-4513; to specify an aim to obtain equal distribution of the subjects in the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported